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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,793	07/08/2005	Alexander Domling	62661(52171)	9957
21874 7590 12/11/2008 EDWARDS ANGELL PALMER & DODGE LLP P.O. BOX 55874 BOSTON, MA 02205				
EXAMINER				
CHANG, CELIA C				
ART UNIT		PAPER NUMBER		
1625				
MAIL DATE		DELIVERY MODE		
12/11/2008		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/520,793

Applicant(s)

DOMLING ET AL.

Examiner

Celia Chang

Art Unit

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 September 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19-38 is/are pending in the application.
- 4a) Of the above claim(s) 35-38 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

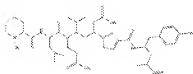
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/CDC)
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____
- Paper No(s)/Mail Date: _____

DETAILED ACTION

1. Applicant's election with traverse of Group I, species as



in the reply filed on May 7, 2008 and Sept. 10, 2008 is acknowledged. The traversal is on the grounds that the PCT search was made on the entire application. This is not found persuasive because the international searches were made on claims 1-5, and 7-8 in part. And anticipatory compounds were found in the search report. Therefore, restriction in accordance to 37 CFR 1.449 and PCT 13.2 Annex Part 1(f)v is proper.

The requirement is still deemed proper and is therefore made FINAL.

Claim 24, $n=4$ (R^2-R^3 forms piperidine) and A is 2-thiazolyl and claims 19-23, 25-34 reading the the elected claim 24, $n=4$ are prosecuted. Claims 35-38 and the remaining subject matter of claims 19-34 (not reading on $n=4$, A=2-thiazolyl) are withdrawn from consideration per 37 CFR 1.142(b).

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 19-33 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Gerhard et. al. DE 10,008,089.

See p.5 compound 1.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that

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the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

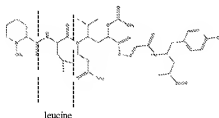
Claims 19-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over DE 10,008,089 or DE 19,638,870 in view of Noren et al.

Determination of the scope and content of the prior art (MPEP §2141.01)

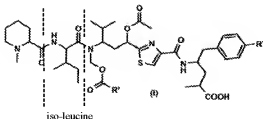
DE 10,008,089 or DE 19,638,870 disclosed Tubulysins having similar structure as the elected species (see '089 fig. 2 or '870 fig. 1-3).

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instantly elected species or claims and the prior art compound is that the instant claims are drawn to:



While the prior art has the same compound where the leucine is iso-leucine:



Finding of prima facie obviousness—rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art would find the above compounds prima facie obvious over the prior art compounds because it is well recognized that the tubulysins are

isolated form culture of mycobacteria. Noren et al. disclosed that both leucine and isoleucine are essential nutrients for culturing mycobacter. The incorporation of alternative essential amino acid in a cultural product is prima facie obvious. While the major component compounds were isolated and delineated in the prior art, the existence and obvious variation of the major components was found since both leucine and isoleucine starting material are available to the culture media. It is expected that the difference of position of methyl between the elected compounds and the prior art compound would exhibit analogous activity in the pharmaceutical art since position isomerism has been used as a tool to obtain new and useful drugs Ex. parte Engelhardt 208 YSPQ 343; In re Mehta 146 USPQ 28784. In the instant case, the position isomeric nutrient is well available to the culture organism.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang, Ph. D. whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres, Ph. D., can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
Dec. 8, 2008

/Celia Chang/
Primary Examiner
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